Anticoagulant Therapy in Postoperative Venous Thrombosis

J. WILLIAM HINTON, *New York*

THROMBO-EMBOLIC disease of the venous system following surgical procedures has attracted tremendous interest among internists and surgeons during the past decade.

Ochsner [10] has divided thrombo-embolic diseases into two groups: Thrombophlebitis and phlebothrombosis, and this classification has been of real clinical help.

Thrombophlebitis is characterized by infection in the vein accompanied by perivenous lymphangitis. This disease is easily recognized clinically because the patients present an elevation of temperature, redness and swelling of the leg, and redness occasionally along the course of the vein.

The treatment of this type of venous thrombo-embolic disease is relatively simple. With elevation of the extremity and rest, plus the use of anticoagulants, fatal pulmonary emboli seldom occur.

Phlebothrombosis is characterized by a clot in the small venules which gradually travels upward. Very little perivascular inflammation is noted. The temperature is very slightly elevated and the condition is frequently not recognized until a fatal embolism has resulted. The mechanism of this type of thrombo-embolic disease is not altogether clear. Bancroft [4] in reviewing 2,000 surgical cases stated that the patients fall in the so-called clotting group having a high prothrombin and fibrinogen index. Loewe [9] stresses the significance of clumping of erythrocytes in the dilated arterioles, which he attributed to the loss of plasma in the highly permeable vascular wall. He refers to these stranded red cells as a sludge. He also emphasizes that the blood platelet count rises rapidly in the immediate postoperative period and the platelets become hyperadhesive, reaching the maximum about ten days after the operation. All these mechanisms would contribute, of course, to the formation of intravascular clots in the small venules, which may extend to the larger veins.

Early detection of phlebothrombosis is difficult. If a patient has a minimal elevation of temperature and every other source for such a temperature has been excluded, then the presence of an intravascular clot should be suspected. Homans [7] has drawn attention to the fact that if the foot is hyperextended, causing extension of the gastrocnemius muscle, the patient complains of pain in the calf, whereas when lying normally he is unaware of any discomfort. This is a simple test and should be done by the resident staff or the attending surgeon on any patient who may run an unexplained minimal temperature.

Read as a part of the Panel Discussion of What's New before the general meeting at the 77th Annual Session of the California Medical Association in San Francisco, April 11-14, 1948.

All surgeons realize the seriousness of venous thrombosis which, if unrecognized, frequently results in sudden death. In a report of 1,665 cases of thrombo-embolic disease developing in surgical patients at the Mayo Clinic,[5] it was found that in 405, or 24.3 per cent, pulmonary embolism occurred in the absence of clinical or necropsy evidence of venous thrombosis. This report included 135 cases of fatal embolism, 87 of which came to autopsy. These figures indicate the importance of early diagnosis and prompt therapeutic procedures to eliminate the venous thrombosis.

From the report of the Mayo Clinic,[5] it is obvious that early diagnosis of venous thrombo-embolic disease is difficult. In only 1,260 of a total of 1,665 cases was the diagnosis made either clinically or at autopsy. In the remaining 405 cases or 24.3 per cent in which pulmonary embolism occurred there was no clinical or necropsy evidence of venous thrombosis. This suggests that the entire thrombus became detached.

TREATMENT

Neither medical nor surgical management of venous thrombo-embolic disease is clear-cut. There are those who advocate early surgical treatment and others who rely exclusively on anticoagulants.

Anticoagulation therapy may take any of the following forms:

1. Heparin intravenously.
2. Heparin subcutaneously.
3. Heparin in Pitkin's menstruum.
4. Heparin and Dicumarol.
5. Dicumarol alone.

Heparin intravenously is not generally used because a continuous intravenous infusion requires constant nursing supervision and recording of the clotting time every hour or every two hours. This form of treatment is expensive and difficult to administer.

Bauer [6] and Jorpes [8] of Sweden administered Heparin subcutaneously every three hours without any ill effect. Fifty to 70 mg. of Heparin may be given, the amount depending on the weight of the patient. Clotting time tests by the Lee-White technique should be done before administration of Heparin, a half hour afterwards, and preferably two and a half hours later. However, the Swedish investigators do not observe clotting times so carefully, and they report no ill effects. A high elevation in the clotting time usually occurs within 30 minutes after subcutaneous injection and the clotting time will usually reach 15 to 20 minutes before the three-hour period has elapsed.

The Pitkin menstruum advocated by Loewe,[9] consisting of Heparin in 18 per cent gelatin, 8 per cent

dextrose, 0.5 per cent glacial acetic acid with distilled water to make 100 per cent, can be given subcutaneously. Loewe advocates using 300 mg. subcutaneously every two days, but some individuals are hyperreactive and others are hyporeactive and therefore variation of the dosage may be necessary. Some individuals who weigh much more than 150 pounds and are hyporeactive are given 400 mg.; very thin people, who may be hyperreactive, are given 200 mg. The clotting time by this method can be kept at 30 minutes. Objections to this method of treatment are that it is painful, that abscesses occasionally develop as a result of the injections, and that it is very expensive.

Heparin and Dicumarol may be administered simultaneously. Heparin in a dosage of 50 to 70 mg. given subcutaneously every three hours for 18 to 24 hours, and Dicumarol given by mouth in a dosage of 300 mg. and then reduced to 200 mg. or less, will usually give the desired result.

Dicumarol given alone may be quite satisfactory in those patients who have a true thrombophlebitis and for whom rapid anticoagulation therapy is not necessary. If this method is used the prothrombin activity should be determined by the Quick or Link-Shapiro method, and the clotting time by the Lee-White technique. The first day, 300 mg. of Dicumarol is given and the prothrombin activity determined. Then the dosage can be regulated. The patient should receive 300 mg. of Dicumarol orally once a day until the prothrombin time is 30 seconds, and 100 to 200 mg. if the prothrombin time exceeds 35 seconds. If it exceeds 60 seconds, 72 mg. of Vitamin K should be given intravenously. This will usually bring the clotting time down without difficulty. If a transfusion is given for supportive reasons, the 300 mg. dose of Dicumarol should be given after the transfusion has been completed. One objection to this method is the development of marked susceptibility to the drug; and bleeding tendencies are not uncommon. In patients in the older age group with arteriosclerosis, the drug must be used with extreme caution.

Surgical operation does have a place in the treatment of thrombo-embolic disease of venous origin, and in patients who have repeated pulmonary emboli, interruption of the venous return may be desirable. One of the difficulties in surgical treatment is determination of the exact site of the thrombosis. Some surgeons advocate superficial femoral ligation[1] and also deep femoral ligation.[2] Recently ligation of the vena cava has been advocated.

Experience with patients who really need vein ligation for thrombo-embolic disease has led the author to the opinion that ligation of the vena cava is preferable to other procedures, as it is the only sure means of entering well above the thrombus.

In the Mayo Clinic report[5] 18 (6.6 per cent) of 273 patients with ilio-femoral thrombophlebitis, clinically diagnosed, died of pulmonary embolism. This experience raises a question as to the treatment of choice. Autopsy revealed that in four of these 18 cases, the fatal embolism occurred from 11 to 32 days after the onset of the disease and the embolism came from a fresh thrombus in the opposite ilio-femoral vein. These statistics plus the recent observations of Allen[3] on 1,180 patients operated upon, half of whom were given Dicumarol and the other half not, gives reason for considering anticoagulant therapy for all patients operated upon. Allen found that there were 75 per cent fewer cases of thrombo-embolic disease among the 580 patients given Dicumarol than there were in the 580 not given the drug. There were two deaths from hemorrhage in the group given Dicumarol, but no deaths from pulmonary embolism.

It may be concluded, therefore, that vena cava ligation is preferable in cases needing surgical interruption of the venous system, and that anticoagulant therapy might be indicated as a routine postoperative measure.

130 East 79th Street.

REFERENCES

1. Allen, A. W., Linton, R. R., and Donaldson, G. A.: Venous thrombosis and pulmonary embolism: Further experience with thrombectomy and femoral vein interruption, Jour. A.M.A., Vol. 128, 1945.

2. Allen, A. W., Linton, R. R., and Donaldson, G. A.: Venus thrombosis and pulmonary embolism, Jour. A.M.A., Vol. 133, 1947.

3. Allen, A. W.: Personal communication.

4. Bancroft, F. W.: A review of the various methods used in the treatment of phlebothrombosis of the extremities, N. Y. State Journal of Med., Vol. 46, February, 1946.

5. Barker, N. W., Nygaard, K. K., Walters, W., and Priestley, J. T.: A statistical study of postoperative venous thrombosis and embolism, Proc. Staff Meet., Mayo Clinic, Vol. 16, 1941.

6. Bauer, G.: Heparin in venous thrombosis, Jour. of A.M.A., Vol. 131, 1946.

7. Homans, J.: Varieties of thrombophlebitis of limbs; their origin, course, and treatment, Amer. Jour. of Surg., Vol. 44, 1939.

8. Jorpes, J. E.: Anticoagulant therapy in thrombosis, Edinburgh M. J., Vol. 53, 1946.

9. Loewe, Leo, Rosenblatt, P., Hirsch, E.: Venous thromboembolic disease, Journal of the Amer. Med. Assoc., February 16, 1946, Vol. 130.

10. Ochsner, A., and DeBakey, M.: Therapy of thrombophlebitis and phlebothrombosis, Archives of Surgery, February, 1940, Vol. 40.